IN THE UNITED STATES PATENT OFFICE

Ex parte Application of Matthew D. IAMMATTEO ("*Premenstrual Dysphoric Disorder Medication*")	Serial No.: unassigned Filing Date: 6 May 04

PETITION

PETITION TO
ACCELERATE EXAMINATION

This is a Petition to accelerate examination pursuant to 37 C.F.R. §1.102 and MANUAL OF PATENT EXAMINING PROCEDURE § 708.02 (VIII).

Issue to be Decided

Whether the Office may accelerate examination of the immediate application?

Relief Requested

Applicant would like the Office to accelerate examination of the immediate application.

Statement of Relevant Facts

1. Applicant here provides a listing of the references identified, together with a detailed discussion pointing out with the particularity required by Rules 111(b) and (c), how the claimed subject matter is patentable over the references. To enable the Office to appreciate how the claimed invention distinguishes over the prior art, we first discuss the art generally, and discussing specifically the most-relevant references identified (copies of these references are attached). We then turn to the immediate claims, and discuss how the immediate claims differ from the teachings of the art. We conclude by reviewing the scope of the various prior art searches made, and mentioning several references provided for background only.

The Art Generally

2. The immediate application is directed to a new way to treat premenstrual dysphoric disorder, the predominately psychological or emotional impairment associated with premenstrual syndrome.

3. The art teaches that the exact cause of premenstrual dysphoric disorder is not completely understood. The puzzle of how to treat the emotional-impairment aspects of premenstrual dysphoric disorder has generated two competing theories regarding the causes of the emotional-impairment aspects of premenstrual dysphoric disorder.

4. One theory postulates that premenstrual dysphoric disorder symptoms are caused by changes in the levels of serotonin, a brain chemical. Another theory postulates that the hormones progesterone, estrogen and testosterone are involved. Each of these two competing theories have undergone some investigation and testing.

Progesterone Has Been Tested

5. Katrina WYATT *et al.*, *Efficacy of Progesterone and Progestens in Management of Premenstrual Syndrome*, 323 BMJ 776 (2001), is a systematic review summarizing the published research investigating progesterone in the management of premenstrual syndrome. WYATT *et al.* (2001) teaches away from the use of hormone in treating premenstrual disorders, concluding that there is "no clinically important difference between progesterone and placebo."

SSRI Has Been Tested

6. Ellen W. FREEMAN *et al.*, *Continuous or Intermittent Dosing With Sertraline for Patients With Severe Premenstrual Syndrome or Premenstrual Dysphoric Disorder*, 161 AM. J. PSYCHIATRY 343 (Feb. 2004) reports, "seratraline groups improved significantly more than the placebo group." FREEMAN (2004) does not mention use of SSRI pharmaceuticals cojointly with estrogen nor progesterone alone, nor in combination. Note that this publication does not qualify as prior art, because it was published in February 2004. FREEMAN (2004) confirms, however, that as recently as February 2004, the art had not recognized that the combination of SSRI pharmaceutical together with estrogen and progesterone may be effective.

7. Katrina M. WYATT *et al.*, *Selective Serotonin Reuptake Inhibitors for Premenstrual Syndrome*, 1 COCHRANE DATABASE OF SYSTEMATIC REVIEWS 2004 is a review which surveys the

art relating to the use of SSRI pharmaceuticals to treat premenstrual syndrome. Note that while this survey carries a publication date of 2004, it appears to have been first published not later than 2002 (in the COCHRANE DATABASE OF SYSTEMATIC REVIEWS Issue No. 4). The earlier version of this review thus appears to qualify as prior art. WYATT (2004) provides an encyclopedic enumeration of the published literature relating to using SSRI pharmaceuticals to treat premenstrual syndrome, citing "Thirty-one published trials were identified which used selective serotonin reuptake inhibitors in the management of premenstrual syndrome." Id. at Page 5 of 30. Of these thirty-one published studies, none teach use of an SSRI pharmaceutical in conjunction with estrogen alone, nor progesterone alone, nor with estrogen and progesterone together.

8. Ellen W. FREEMAN *et al., Differential Response to Antidepressants in Women With Premenstrual Syndrome*, 56 ARCH. GEN. PSYCHIAT. 932 (1999) (Abstract only) compares the efficacy of various antidepressants in treating premenstrual dysphoric disorder. FREEMAN (1999) does not suggest, nor even mention, use of estrogen nor progesterone.

SSRI and Progesterone Have Been Compared, but not Combined

9. Ellen W. FREEMAN *et al.*, *A Double-Blind Trial of Oral Progesterone, Alprazolam and Placebo in Treatment of Severe Premenstrual Syndrome*, 274 JAMA 343 (5 July 1995), tests these two competing theories. FREEMAN *et al.* (1995) thus compares the effectiveness of Alprazolam (an antidepressant) alone, or progesterone alone, on premenstrual dysphoric disorder symptoms. FREEMAN *et al.* (1995) finds that alpazolam shows a 50% reduction in "daily symptom report scores: the authors thus conclude that, "Alprazolam has a role in PMS treatment." In contrast, FREEMAN *et al.* expressly teaches away from the use of hormones, teaching that "progesterone therapy was no better than placebo" and concluding rather flatly, "progesterone is ineffective for PMS." Pointedly, the reference does not mention estrogen at all. Further, while FREEMAN (1995) tests alprazolam and progesterone individually, it neither tests the two in combination, nor suggests combining the two.

10. *ACOG Issues Guidelines On Diagnosis and Treatment of PMS* (31 March 2000) (The American College of Obstetricians and Gynecologists, Washington DC, publ.), says the same

thing. The reference teaches that "Serotonin selective reuptake inhibitor (SSRIs) antidepressants have been shown effective and may be useful for severe PMS." In contrast, however, *ACOG Issues Guidelines...* does not teach the use of such an SSRI pharmaceutical in combination with estrogen alone, nor progesterone alone, nor with estrogen and progesterone together. To the contrary, the reference teaches away from using estrogen nor progesterone, because it implies that these hormones are ineffective despite wide testing ("Oral contraceptives have been widely prescribed as a treatment for PMS, but there is little data to support their effectiveness.").

11. The art does, however teach combining an antidepressant with a growth hormone secretagogue. Welch Willard MCKOWAN *et al.*, WO/01 89570 A2 (also available as published USA application No. US20000207017P) teaches a combination of antidepressant and "growth hormone secretagogues." MCKOWAN *et al.* does not teach combining an antidepressant with a hormone *per se*, but with a hormone-secretion stimulant (growth hormone secretagogue). MCKOWAN does not, however teach combining antidepressant with estrogen nor progesterone. Further, the utility of MCKOWAN's combinations is different than that of the claimed combinations.

The Immediate Claims

12. In contrast to the prior art, Applicant has found that the constellation of symptoms can be treated most effectively by addressing serotonin levels and hormone levels conjointly. In contrast to the prior art, which has focused on SSRI pharmaceuticals alone, and which teaches away from using hormones such as progesterone or estrogen, Applicant has tested SSRI pharmaceuticals conjointly with estrogen and progesterone as a premenstrual dysphoric disorder therapeutic, and found that the combination provides several advantages.

13. Application Claim 1 accordingly is drawn to a combination of a SSRI pharmaceutical + estrogen + progesterone. Claim 1 (emphasis added) reads:

> 1. A product for treating premenstrual dysphoric disorder, comprising:
> a. a hormone comprising estrogen and progesterone; and
> b. a selective serotonin reuptake inhibitor;
> c. said estrogen and said progesterone present in amounts which together are effective as a contraceptive; and

d. said selective serotonin reuptake inhibitor present in an amount effective to reduce emotional impairment related to premenstrual dysphoric disorder, when administered with said hormone.

The Searches

14. A pre-examination search was made; more precisely, two searches were made. One search encompassed United States patents and published patent applications, as well as PCT applications published internationally under the Patent Cooperation Treaty. The other search encompassed the non-patent medical literature.

15. The patent search patents included a search for published PCT applications which mention the terms "serotonin" and "hormone" in the Abstract. Neither of the two applications identified appears germane.

16. The patent search included a search for US patents in International Class A61K, ostensibly containing patents drawn to a sex hormone (*e.g.*, estrogen) combined with another pharmaceutical (*e.g.*, an antidepressant). No US patents are so classified.

17. The patent search included a search of US patents in US Class 552, subclass 607 (hormone compositions), which mention the term "antidepressant." No such patents appeared.

18. The patent search included a search of US patents which mention the term "contraceptive" and "antidepressant" in the claims. None of the six patents identified appears particularly relevant.

19. The patent search also included a search for published PCT applications which mention the term "antidepressant," "anti-depressant" or "serotonin" in the Abstract, and also mention the term "estrogen" or progesterone" in the abstract. Of the one hundred and fifty one applications identified, the most relevant (indeed, the only application which appears directed to a hormone combined with another pharmaceutical) is Welch Willard MCKOWAN *et al.*, WO/01 89570.

20. The search for non-patent medical literature encompassed a search directed at finding literature review article(s) which enumerate and summarize primary research articles addressing the combination of an SSRI pharmaceutical with estrogen or progesterone, to treat pre-menstrual syndrome. Searching for review articles provides a reliable "meta-search," which takes advantage of the published expertise of those of skill in the art to identify potentially-relevant art.

This approach thus reduces the likelihood that any specific primary research article will not be identified by the search.

21. We include here several references which provide general background information on hormone therapy, hormones useable as contraceptives, and pharmaceutical formulation technology. Applicant does not believe that these references bar the claims; to the contrary, these references provide evidence of the level of skill in the art, and thus supplement Applicant's the disclosure under 35 USC 112.

22. DEBREGEAS *et al.*, United States Letters Patent No. 4,960,596, teaches one approach to avoid adverse chemical reactions between the various pharmaceutical components. DEBREGEAS teaches that one or several of the substances can be provided as a core of active ingredient, which core is built up or coated with a barrier which remains chemically inert until the product is used.

23. United States Letters Patent No. 5,529,791 (25 June 1996) teaches an alternative approach, wherein the various drug substances are mixed with an inert compound which provides an inert matrix separating the various drug substances until ingested.

24. SHANGOLD *et al.*, United States Letters Patent No. 6,214,815, teaches contraceptive-effective amounts of hormones.

25. CUMMINGS *et al.*, United States Letters Patent No. 6,692,763 (14 Feb. 2004), teaches hormone replacement therapy effective amounts of estrogen.

Summary

Applicant presents only two independent claims: claim #1 and claim #17. Both independent claims (and the claims depending there from) are believed directed to a single invention.

Enclosed find the fee set forth in 37 CFR 1.17(h), and one copy of each of the references discussed.

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Enclosures

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